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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,149	01/23/2007	David N. Watkins	JHU2050-1	5576

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DLA PIPER LLP (US)
4365 EXECUTIVE DRIVE
SUITE 1100
SAN DIEGO, CA 92121-2133

EXAMINER	
HUFF, SHEELA JITENDRA	
ART UNIT	**PAPER NUMBER**
1643	
MAIL DATE	**DELIVERY MODE**
10/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,149	WATKINS ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *24-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-23 in the reply filed on 8/25/08 is acknowledged.

Priority

The instant set of claims has priority to 10/20/04 and not to the provisional application because the provisional application only discloses hedgehog inhibitors and does not specifically mention agonists and antagonists. Additionally, the limitations of claims 10-11 and 20-21 are not mentioned in the provisional application.

Claim Objections

Claim 4 is objected to because of the following informalities: The word "patway" should be --pathway--.. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear what the antibody or binding fragment thereof are meant to bind.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-7 and 13-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Watkins et al Nature vol. 422 p. 313 (3/20/03) as evidenced by Zhang et al Bioorganic and Medicinal Chemistry Letters vol. 18 p. 1359 (2008).

This reference discloses the use of the steroid alkaloid cyclopamine and KAAD cyclopamine to inhibit the hedgehog signaling pathway in small cell lung cancer (SCLC). This inhibition effect is only seen in SCLC cells that express both sonic hedgehog and

its transcriptional factor GLi-1 (see page 315--second full paragraph). As shown by Zhang et al, the structure of cyclopamine (figure 1) reads on applicant's invention.

Claims 1-10, 13-20 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/080952.

This reference discloses the use of a modulator of a hedgehog signaling pathway, or a modulator of a pathway which is the target of the hedgehog signaling pathway in the treatment of T-cell proliferation/apoptosis (pages 3-4, 7) and wherein the modulator is an inhibitor/antagonist (page 5 and 11 and 22) and where the treatment can be of small-cell lung cancer (page 90). Specific alkaloids used the treatments include cyclopamine, which blocks the Shh signaling pathway (page 23-25). The antagonists can be proteins, nucleic acids, or antibodies (page 11). These antagonists can be used in combination with other agents such as methotrexate (a chemotherapetuic agent) (page 106). Administration can be oral (page 100).

Claims 1-6, 13-18 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 03/088970 (filed 4/22/02).

This reference discloses methods and reagents for inhibiting the activation of the hedgehog signaling pathway using agents such as small molecules that antagonist the hedgehog activity (page 9). The disease to be treated includes small cell lung cancer (page 11, line 20). The antagonist includes compoudsn that regulate the expression

level of Gli2 genes (pages 15-16). Administration can be oral (page 84). The small compounds of the invention are many and start at page 31 of the reference.

Claims 1-9, 13-20 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Dudek et al US 2004/0060568 (filed 10/13/00).

This reference discloses methods and reagents for the inhibition of undesired growth states that occur in cells with an active hedgehog signaling pathway. These cells overexpress the Gli gene ([0023]). The hedgehog antagonists include antibodies ([0498]) and small molecules (such as cyclopamine) ([0026], [0266] and [0164]+) and hedgehog mutants ([0480]). The cancer to be treated includes small cell lung cancer ([0112]). Administration can be oral ([0609]).

Claims 1-6, 8-18 and 20-23 are rejected under 35 U.S.C. 102(e) as being anticipated by Ling et al US 2005/0054568 (8/23/03).

This reference discloses methods and reagents for the inhibition of undesired growth states that occur in cells with an active hedgehog signaling pathway. These cells overexpress the Gli gene (0010]+ and [0087]). The hedgehog antagonists include antibodies (including hedgehog antibodies) and small molecules (that read on steroidal alkaloid and derivatives thereof) and hedgehog mutants (see entire reference). The antagonists can be used alone or in combination ([0016]). The cancer to be treated includes small cell lung cancer ([0019] and [0614]). Administration can be oral ([0630]). These therapeutics can be used in combination with other chemotherapeutics ([0649]).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 13-19 and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 43-75 of copending Application No. 11/338503. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference between the two sets of claims is the scope of the cancer to be treated. Specifically, the scope of the cancer to be treated in the instant application is narrower than the 503 case because the cancer in the instant case is limited to small cell lung cancer.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-7, 13-19 and 23 are directed to an invention not patentably distinct from claims 43-75 of commonly assigned 11/338503. The reasons have been discussed above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 11/338503, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Tuesday and Thursday from 5:30am to 1:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sheela J Huff/
Primary Examiner
Art Unit 1643

sjh